Structural Analysis of the Telomerase RNA Pseudoknot Domain by Raman Spectroscopy

Vibrational spectroscopy is widely used to probe structural features of proteins, carbohydrates, and nucleic acids by measuring conformational marker bands. In particular, RNA nucleoside and phosphate-backbone conformational markers are indicators of helical conformation and tertiary structure. Since Raman conformational markers are reliably correlated with RNA secondary and tertiary structure, this helps to facilitate the adoption of Raman spectroscopy for the analysis and characterization of a wide range of RNA therapeutic agents. This includes the on-line batch analysis of known candidate therapeutic drugs, such as those being developed to target inhibition of HIV-1 infection.

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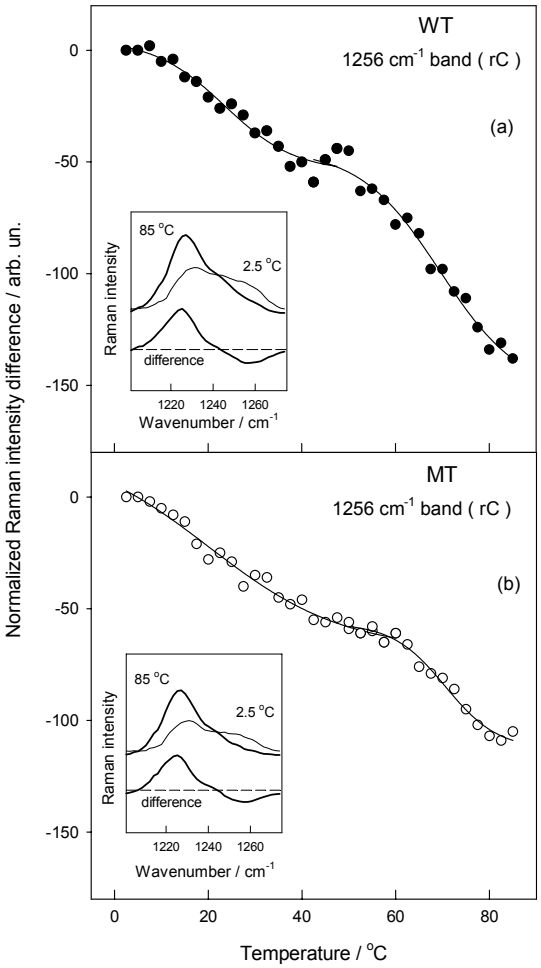
In a recent study at NIST, Raman spectroscopy was used to analyze the pseudoknot region of telomerase RNA (a cancer biomarker). Conformational changes that are caused by the two nucleotide substitutions (mutations) present in the disease *dyskeratosis congenita* (DKC) were detected. We are now using Raman spectroscopy to probe the structure of the template or active site region of telomerase RNA. These newly developed methods will help to facilitate the development of rapid screening tools for the effectiveness of RNA-based cancer therapeutic agents.

Publication

V. Reipa, G. Niaura, and D. H. Atha, ***"Structural analysis of the telomerase RNA pseudoknot domain by Raman spectroscopy,"*** *RNA*, submitted.



Temperature-dependent profiles of the 1256 cm^{-1} Raman band, assigned to cytosine nucleotides with C2'-endo/anti sugar puckers for the wild-type (a) and DKC-mutated (b) hairpin oligonucleotides.